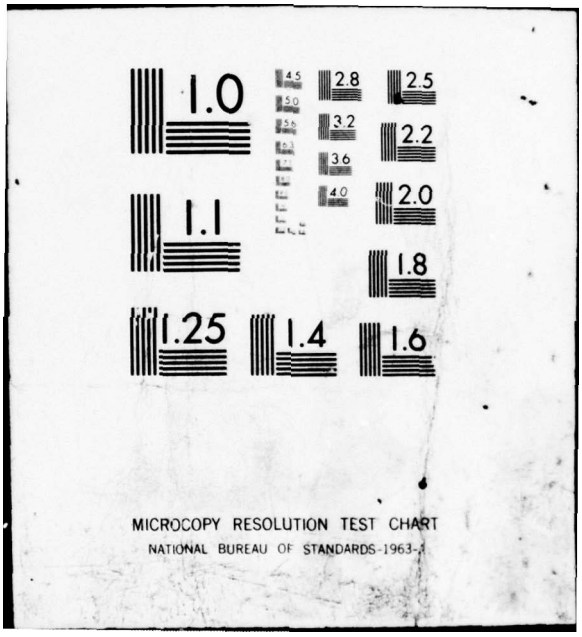
AD-A067 273 FLORIDA STATE UNIV TALLAHASSEE DEPT OF STATISTICS F/G 12/1
A BAYESIAN APPROACH TO BIOASSAY.(U)
FEB 79 D BASU, R FAGERSTROM NSF-MCS77-01661
UNCLASSIFIED FSU-STATISTICS-M498 ARO-13888.16-MX NL

| OF |
AD
A067 273

END
DATE
FILMED
6 -79
DDC


1.0
1.1
1.25
1.4
1.6
1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0
4.5
5.0
MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

ARO 13888.16-MX

(12) (18) (19)

LEVEL II

(6) A BAYESIAN APPROACH TO BIOASSAY.

by

(10) D. Basu[1] and Richard Fagerstrom[2]

(14) FSU-STATISTICS-M498, TR-D32

(12) 16 p.

FSU Statistics Report M498
(9) Technical Report, USARO-D32

(11) Feb[redacted]979

Department of Statistics
The Florida State University
Tallahassee, Florida 32306

(15) NSF-MCS77-01661, DAAG29-76-G-0238

1. Research supported by National Science Foundation Grant No. MCS 77-01661.

2. Research supported by the United States Army Research Office, Durham, under Grant No. DAAG29-76-G-0238.

A Bayesian Approach to Bioassay

by

D. Basu and Richard Fagerstrom
(The Florida State University)

ABSTRACT

This article explains in general terms how some sequential bioassay methods like the stochastic approximation method or the up-and-down method are not in conformity with the likelihood principle. Irrespective of the sampling plan, the bioassay data may be analyzed in terms of the following simple prior probability model for the response probabilities.

Let $x_1' < x_2' < \ldots < x_m'$ be the distinct dosage levels used in a bioassay experiment and let $P_1 < P_2 < \ldots < P_m$ be the corresponding unknown response probabilities. Let $U_1 = P_1$ and $U_i = (P_i - P_{i-1})/(1 - P_{i-1})$, $i = 2, 3, \ldots m$. The U_i's are regarded as mutually independent random variables taking values in the unit interval. The P_i's then form a Markov chain. The means and the variances of the P_i's are related to those of the U_i's in a rather simple fashion. The case where $U_i \sim$ Beta$(1, \lambda_i)$ is found to be particularly tractable for the analysis of bioassay data.

1. INTRODUCTION

This report is concerned with the following problem of quantal-response bioassay. In the background there is a sequence of i.i.d. random variables $Z_1, \ldots, Z_N$ which are not directly observable and have common c.d.f. F. Even though each Z_i is unobservable, it is possible to verify for any fixed $x_i \in R$ whether $Z_i \leq x_i$, i.e. we can observe for each i

$$Y_i(x_i) = I_{\{Z_i \leq x_i\}}.$$

The parameter of interest is $\theta_\alpha (0 < \alpha < 1)$, which is assumed to be uniquely defined by the equation $F(\theta_\alpha) = \alpha$.

From a biological standpoint we consider a population of individuals which may be subject to a stimulus. For each member there exists a threshold dose of the stimulus above which the individual responds and below which it does not. Therefore, the threshold dose Z for a randomly selected subject is a random variable with a c.d.f. F. Experimentation is conducted through the selection of N subjects, for which the threshold doses are $Z_1, \ldots, Z_N$, and the testing of the i^{th} $(i = 1, \ldots, N)$ subject for response to a dose level x_i of the stimulus. We wish to estimate the dose to which a proportion α of the population will respond, which is θ_α.

2. SOME SEQUENTIAL DESIGNS

In pursuit of a solution to this problem, a variety of designs and corresponding analyses has been proposed. Sequential methods have received close theoretical attention. Among the most prominent are stochastic approximation and the up-and-down method and its modifications. According

to the theory of stochastic approximation, the x_i's are selected in the following manner: x_1 is picked by the experimenter and

$$x_{i+1} = x_i + a_i(\alpha - Y_i(x_i)) \quad \text{for} \quad i \geq 1,$$

where the a_i's are positive real numbers such that

$$\sum_{i=1}^{\infty} a_i = \infty \quad \text{and} \quad \sum_{i=1}^{\infty} a_i^2 < \infty,$$

and x_{N+1} is the estimator of θ_α after N steps. The design may be modified in a straightforward manner to accommodate the case of multiple observations at each step. Theorems by Blum [3] and Sacks [6] may be invoked to prove strong consistency and asymptotic normality, respectively, of the estimator.

The method of stochastic approximation assumes that arbitrarily small adjustments of the dose may be performed. However, the set of possible doses is finite in any experimental situation because of limitations of the measuring instruments. A sequential design which takes this fact into consideration is the random walk design, used in the estimation of $\theta_{\frac{1}{2}}$. It is described in its most general form by Tsutakawa [7]. In this design x_1 is selected by the experimenter and for $i \geq 1$

$$x_{i+1} = \begin{cases} x_i + d & \text{if} \quad 0 \leq R_i \leq k \\ x_i & \text{if} \quad k < R_i < n - k \\ x_i - d & \text{if} \quad n - k \leq R_i \leq n, \end{cases}$$

where d is a positive real number, n is the number of observations at each x_i, R_i is the number of responses at x_i, and k is an integer such that $0 \leq k < \frac{n}{2}$. For $n = 1$ and $k = 0$ this design is commonly known as the up-and-down method. When sampling is terminated after N steps, Tsutakawa uses the statistic

$$\bar{x}_N = \frac{1}{N} \sum_{i=2}^{N+1} x_i$$

for estimating $\theta_{\frac{1}{2}}$. While this estimator is not consistent, Tsutakawa claims that for symmetric continuous F, $|\lambda - \theta_{\frac{1}{2}}| \leq d/2$, where λ is the almost-sure limit of $\bar{x}_N$ as $N \to \infty$. This is sufficiently close from a practical point of view.

Modifications of the up-and-down method have been proposed for the purpose of estimating general θ_α. One such modification is due to Derman [4]. In his design the choice of x_1 is left to the experimenter and for $i \geq 1$

$$x_{i+1} = \begin{cases} x_i - d \text{ with probability } \frac{1}{2\alpha} & \text{if } Y_i(x_i) = 1 \\ x_i + d \text{ with probability } 1 - \frac{1}{2\alpha} & \text{if } Y_i(x_i) = 1 \\ x_i + d & \text{if } Y_i(x_i) = 0 \end{cases}$$

for $\frac{1}{2} \leq \alpha < 1$. The alterations for $0 < \alpha < \frac{1}{2}$ are straightforward. Derman estimates θ such that $F(\theta - 0) \leq \alpha \leq F(\theta)$ by θ_N, the most frequent value of x in N steps or the arithmetic mean of such values if there are ties, and proves the following theorem:

Theorem. If F(x) is increasing on $[\theta - d, \theta + d]$, then $\Pr\{\max\{|\overline{\lim}\ \theta_N - \theta|, |\underline{\lim}\ \theta_N - \theta|\} < d\} = 1$.

Note that none of the methods discussed above makes use of the likelihood function in obtaining an estimator for θ_α. This fact places them out of full compliance with one of the tenets of Bayesianism, the likelihood principle, as we shall see in the next section.

3. THE LIKELIHOOD PRINCIPLE

Before determining the likelihood function generated by quantal-response data, some notation will be defined. Let $x_1' < \ldots < x_m'$ be the distinct dose levels, let n_i be the number of times that x_i' is selected, i.e.

$$n_i = \sum_{j=1}^{N} I_{\{x_i'\}}(x_j),$$

and let R_i be the number of responses at dose level x_i', i.e.

$$R_i = \sum_{\{j: x_j = x_i'\}} Y_j(x_j).$$

If we define $P_i = F(x_i')$ and let r_i be a realization of R_i, then the likelihood function generated by the data is

$$\prod_{i=1}^{m} \binom{n_i}{r_i} P_i^{r_i} (1 - P_i)^{n_i - r_i} I_{\{0,\ldots,n_i\}}(r_i).$$

Accordingly, the full data $\{Y_i(x_i): i = 1, \ldots, N\}$ may be summarized by the statistic $\{(x_i', n_i, R_i): i = 1, \ldots, m\}$. The sampling plan is not detectable in the likelihood function. This recognition forms the germ of the likelihood principle, which, as discussed in [2], says that two sets of data generating equivalent likelihood functions contain the same relevant information about the parameter. Two likelihood functions are said to be equivalent if one is a constant multiple of the other, where the constant may depend on the data. According to this principle, statistical inference should be based on the whole of the relevant information about the parameter supplied by the data, this information being contained in the likelihood function. Average performance characteristics, such as asymptotic properties, are irrelevant at the data analysis stage. It is seen that the estimators associated with the designs in Section 1 are not fully in keeping with the likelihood principle, since they are justified by asymptotic properties and do not employ the totality of the useful information in the likelihood function.

4. A CONJUGATE PRIOR FAMILY

In order to abide by the likelihood principle, a Bayesian approach will be adopted. It will not be assumed that F belongs to a parametric family of c.d.f.'s. Since a conjugate prior distribution possesses the appealing property that the posterior distribution is of the same form, let us first consider a family of conjugate priors for $(P_1, \ldots, P_m)$. The p.d.f. associated with each distribution of this family has the following form:

$$g(p_1, \ldots, p_m) = C\Big(\prod_{i=1}^{m} p_i^{\alpha_i - 1} (1 - p_i)^{\beta_i - 1}\Big) I_E(p_1, \ldots, p_m),$$

where the α_i's and β_i's are real numbers such that

$$\sum_{i=1}^{j} \alpha_i > 0 \text{ and } \sum_{i=j}^{m} \beta_i > 0 \text{ for } j = 1, \ldots, m,$$

C is a constant ensuring that $\int g(p_1, \ldots, p_m)dp_1 \ldots dp_m = 1$, and $E = \{(p_1, \ldots, p_m): 0 \le p_1 \le \ldots \le p_m \le 1\}$. Given values of $r_1, \ldots, r_m$ for $R_1, \ldots, R_m$, respectively, the posterior p.d.f. of $(P_1, \ldots, P_m)$ has the form

$$\frac{1}{S(r_1, \ldots, r_m)} \prod_{i=1}^{m} p_i^{\alpha_i + r_i - 1} (1 - p_i)^{\beta_i + n_i - r_i - 1} I_E(p_1, \ldots, p_m).$$

Unfortunately, the computation of prior and posterior means, which are commonly used Bayesian estimators, is a tedious procedure inclined to yielding cumbersome expressions. For instance, the posterior mean of P_i for $i = 1, \ldots, m$ in the relatively simple case of α_i a positive integer for all i is

$$1 - \frac{1}{S(r_1, \ldots, r_m)} \sum_{j_1=0}^{\alpha_1+r_1-1} \cdots \sum_{j_m=0}^{\alpha_m+r_m-1} \left[\prod_{k=1}^{m} \binom{\alpha_k + r_k - 1}{j_k} \right] (-1)^s \times$$

$$\left(\prod_{j=1}^{i} B\left(1, \sum_{k=j}^{m} (\beta_k + n_k - r_k + j_k) + 1\right) \right) \prod_{j=i+1}^{m} B\left(1, \sum_{k=j}^{m} (\beta_k + n_k - r_k + j_k)\right),$$

where $S(r_1, \ldots, r_m) = \sum_{j_1=0}^{\alpha_1+r_1-1} \cdots \sum_{j_m=0}^{\alpha_m+r_m-1} \left[\prod_{k=1}^{m} \binom{\alpha_k + r_k - 1}{j_k} \right] (-1)^s \times$

$$\prod_{i=1}^{m} B\left(1, \sum_{k=i}^{m} (\beta_k + n_k - r_k + j_k)\right),$$

$s = \sum_{k=1}^{m} j_k$, $B(\alpha, \beta)$ is the beta function with parameters α and β, and

$\prod_{j=m+1}^{m} B\left(1, \sum_{k=j}^{m} (\beta_k + n_k - r_k + j_k)\right)$ is defined to be 1. The formulae for the prior and posterior variances of the P_i's are conjectured to be at least as unattractive.

5. ISOTONIC REGRESSION METHOD

Realizing the complexity of the expressions for the prior and posterior means of $(P_1, \ldots, P_m)$, one may at first be inclined to divert attention to other Bayesian estimates of this vector such as the prior and posterior modes. Indeed, these estimates may often be obtained relatively easily by way of an isotonic regression, the definition of which is stated below as in [1].

Definition. Suppose that X is a finite set on which is defined a simple order "$\prec$". A real-valued function f defined on X is said to be isotonic if

for all $x, y \in X$ such that $x \prec y$, $f(x) \leq f(y)$. For a specified function g on X and a specified positive function w on X, an isotonic function g^* on X which minimizes

$$\sum_{x \in X} [g(x) - f(x)]^2 w(x)$$

in the set of isotonic functions f on X is an isotonic regression of g with weights w with respect to the simple order "$\prec$".

The following theorem from [1] permits the use of isotonic regression for determining modes of certain distributions in the conjugate family.

Theorem. Let g be a function defined on X, w be a positive function on X, Φ be a convex function that is finite on an interval I enclosing the range of g and infinite elsewhere, and ϕ be the right derivative of Φ. Then g^* (defined as previously) maximizes

$$\sum_{x \in X} [\Phi(f(x)) + (g(x) - f(x))\phi(f(x))]w(x)$$

in the class of isotonic functions f on X with range in I.

Let us now see how this theorem may be applied to maximize a function of the form

$$\prod_{x=1}^{m} p_x^{\alpha_x - 1} (1 - p_x)^{\beta_x - 1}$$

with respect to $p_1, \ldots, p_m$ under the order restriction $0 \leq p_1 \leq \ldots \leq p_m \leq 1$ when $\alpha_x \geq 1$, $\beta_x \geq 1$, and $\alpha_x + \beta_x - 2 > 0 \ \forall x$. The latter restrictions ensure the existence of a maximum. Maximizing this function is equivalent to maximizing its natural logarithm, which is

$$\sum_{x=1}^{m} [(\alpha_x - 1)\ln p_x + (\beta_x - 1)\ln(1 - p_x)].$$

We then utilize the above theorem by taking $X = \{1, \ldots, m\}$, "$\leq$" as the simple order, $g(x) = \frac{\alpha_x - 1}{\alpha_x + \beta_x - 2}$, $w(x) = \alpha_x + \beta_x - 2$, and

$$\Phi(u) = \begin{cases} u \ln u + (1 - u) \ln (1 - u) & \text{for } 0 < u < 1 \\ 0 & \text{for } u = 0, 1. \end{cases}$$

As an application of the procedure discussed in the preceding paragraph, consider the function

$$p_1^2(1 - p_1)p_2(1 - p_2)^2 p_3^3(1 - p_3),$$

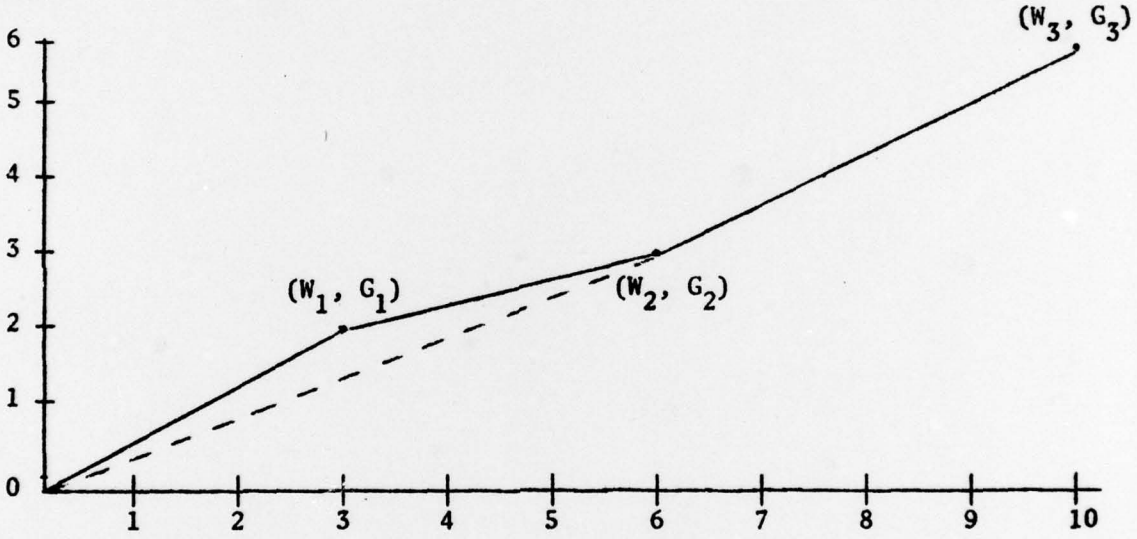
which we wish to maximize subject to the constraints $0 \leq p_1 \leq p_2 \leq p_3 \leq 1$. The values of p_1, p_2, and p_3 yielding this maximum are obtained from the isotonic regression g^* of g with weights w, where g and w are as defined below:

x	$g(x)$	$w(x)$
1	$\frac{2}{3}$	3
2	$\frac{1}{3}$	3
3	$\frac{3}{4}$	4

In determining g^* a graphical approach may be taken. First construct the cumulative sum diagram (CSD), which consists of the points (0, 0), (W_1, G_1), (W_2, G_2), and (W_3, G_3), where

$$W_j = \sum_{x=1}^{j} w(x) \text{ and } G_j = \sum_{x=1}^{j} w(x)g(x) \text{ for } j = 1, 2, 3,$$

and connect its points. Next construct the greatest convex minorant (GCM), which is the graph of the supremum of all convex functions possessing graphs below the CSD and is composed of line segments. Then for x = 1, 2, 3 $g^*(x)$ is the slope of the part of the GCM immediately to the left of the point having abscissa W_x. Hence, we have $g^*(1) = g^*(2) = \frac{1}{2}$ and $g^*(3) = \frac{3}{4}$ as seen on the figure below. The CSD is composed of the solid segments, while the GCM, where it differs from the CSD, is designated by dashed segments.



6. A PRIOR PROBABILITY MODEL

Despite its ease of computation, the joint mode may not be appealing to some as an estimator because of the following possibility: A component of the joint mode may not equal the corresponding marginal mode. To see this, consider the following example. Let the p.d.f. of interest be

$$f_{(P_1,P_2)}(p_1, p_2) = p_1^3(1 - p_1)p_2^2(1 - p_2)^4 I_E(p_1, p_2),$$

where $E = \{(p_1, p_2): 0 \le p_1 \le p_2 \le 1\}$. From isotonic regression the mode of this distribution is (0.5, 0.5). Now, the marginal p.d.f. of P_1 is

$$f_{P_1}(p_1) = p_1^3(1 - p_1)\int_{p_1}^{1} p_2^2(1 - p_2)^4 dp_2$$

$$= p_1^3(1 - p_1)\int_{0}^{1-p_1} p_2^4(1 - p_2)^2 dp_2$$

$$= p_1^3(1 - p_1)B_{1-p_1}(5, 3),$$

where $B_{1-p_1}(5, 3)$ is defined by context. The incomplete beta function with parameters a and b evaluated at x $I_x(a, b) = B_x(a, b)/B(a, b)$ is tabulated in [5]. Using this table we obtain $f_{P_1}(0.5) = (0.5)^4 B_{0.5}(5, 3) = 1.349 \times 10^{-4}$. However, $f_{P_1}(0.4) = (0.4)^3(0.6)B_{0.6}(5, 3) = 1.536 \times 10^{-4}$. Therefore, 0.5 is not the mode of the marginal distribution of P_1.

Since every component of a joint mean does equal the mean of the corresponding marginal distribution, it may be worthwhile to investigate whether the calculation of the prior and posterior means may be simplified by, for example, restructuring the family of priors. Let us begin by considering a sequence $U_1, \ldots, U_m$ of independent random variables taking values in [0, 1]. Define

$$P_1 = U_1,$$

$$P_{i+1} = P_i + (1 - P_i)U_{i+1} \text{ for } i = 1, \ldots, m - 1.$$

Dealing with a prior defined in this manner is not such an unpleasant experience. For example, if $\mu_i = E(P_i)$ and $\nu_i = E(U_i)$ for i = 1, ..., m, then

$$\mu_1 = \nu_1,$$

$$\mu_{i+1} = \mu_i + (1 - \mu_i)\nu_{i+1} \text{ for } i = 1, \ldots, m - 1.$$

Also, if $\rho_i = E(P_i^2)$ and $\tau_i = E(U_i^2)$ for $i = 1, \ldots, m$, then

$$\rho_1 = \tau_1,$$

$$\rho_{i+1} = \rho_i + 2(\mu_i - \rho_i)\nu_{i+1} + (1 - 2\mu_i + \rho_i)\tau_{i+1}$$

for $i = 1, \ldots, m - 1$.

Conversely, one can select the means and perhaps the variances of the U_i's to be concordant with prior opinions about the corresponding moments of the P_i's. This direction will be taken in the next paragraph. Another interesting property of this process is that it is a Markov chain, since for $1 \le i \le m - 1$ P_{i+1} is defined only in terms of P_i and U_{i+1}, which is independent of $P_1, \ldots, P_i$.

For an example of the above method, consider the case in which $U_i \sim \text{Beta}(1, \lambda_i)$ for $i = 1, \ldots, m$. As described in the preceding paragraph, the λ_i's may be chosen to conform with some prior opinion about $E(P_i)$ for $i = 1, \ldots, m$. If it is our opinion that $E(P_i) = \mu_i$ for $i = 1, \ldots, m$, then $\mu_1 = \frac{1}{1 + \lambda_1}$, so that $\lambda_1 = \frac{1 - \mu_1}{\mu_1}$.

Also, for $i = 1, \ldots, m - 1$

$$\mu_{i+1} = \mu_i + (1 - \mu_i)\left(\frac{1}{1 + \lambda_{i+1}}\right).$$

Hence, $\lambda_{i+1} = \frac{1 - \mu_{i+1}}{\mu_{i+1} - \mu_i}$. Now, the joint p.d.f. of $U_1, \ldots, U_m$ is

$$f(u_1, \ldots, u_m) = K \prod_{i=1}^{m} (1 - u_i)^{\lambda_i - 1} I_{[0,1]}(u_i),$$

where $K = \prod_{i=1}^{m} \frac{\Gamma(\lambda_i + 1)}{\Gamma(\lambda_i)} = \prod_{i=1}^{m} \lambda_i$, and $\frac{\partial(u_1, \ldots, u_m)}{\partial(p_1, \ldots, p_m)} = \prod_{i=1}^{m-1} (1 - p_i)^{-1}$; therefore, the joint p.d.f. of $P_1, \ldots, P_m$ is

$$h(p_1, \ldots, p_m) = K(1 - p_1)^{\lambda_1 - 1} \left(\prod_{i=1}^{m-1} \left(\frac{1 - p_{i+1}}{1 - p_i} \right)^{\lambda_{i+1} - 1} \right) \times$$

$$\left(\prod_{i=1}^{m-1} (1 - p_i)^{-1} \right) I_E(p_1, \ldots, p_m),$$

where $E = \{(p_1, \ldots, p_m): \ 0 \leq p_1 \leq \ldots \leq p_m \leq 1\}$. This expression may be rearranged to yield

$$K\left(\prod_{i=1}^{m-1} (1 - p_i)^{\lambda_i - \lambda_{i+1} - 1} \right) (1 - p_m)^{\lambda_m - 1} I_E(p_1, \ldots, p_m).$$

Hence, the family of priors of this form is contained in the conjugate family given on p. 5. The posterior p.d.f. of $(P_1, \ldots, P_m)$ has the form

$$\frac{1}{S(r_1, \ldots, r_m)} \left(\prod_{i=1}^{m-1} p_i^{r_i} (1 - p_1)^{\lambda_i - \lambda_{i+1} + n_i - r_i - 1} \right) p_m^{r_m} (1 - p_m)^{\lambda_m + n_m - r_m - 1} \times I_E(p_1, \ldots, p_m).$$

At present this is the extent of our research into this problem. In the future we shall attempt to represent the posterior distribution in a form which is amenable to the computation of the posterior mean.

REFERENCES

[1] Barlow, R. E., Bartholomew, D. J., Bremner, J. M. and Brunk, H. D. (1972). Statistical Inference under Order Restrictions. John Wiley & Sons, London.

[2] Basu, D. (1975). Statistical information and likelihood. Sankhya, A, 37, 1-71.

[3] Blum, J. R. (1954). Approximation methods which converge with probability one. Ann. Math. Statist., 25, 382-386.

[4] Derman, C. (1957). Non-parametric up-and-down experimentation. Ann. Math. Statist., 28, 795-798.

[5] Pearson, K. (1968) Tables of the Incomplete Beta-Function. Cambridge University Press, Cambridge.

[6] Sacks, J. (1958). Asymptotic distribution of stochastic approximation procedures. Ann. Math. Statist., 29, 373-405.

[7] Tsutakawa, R. K. (1967). Random walk design in bio-assay. J. Amer. Statist. Assoc., 62, 842-856.

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1. REPORT NUMBER FSU No. M498 USARO-D32	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE A Bayesian Approach to Bioassay		5. TYPE OF REPORT & PERIOD COVERED Technical Report 6. PERFORMING ORG. REPORT NUMBER FSU Statistics Report M498
7. AUTHOR(s) D. Basu Richard Fagerstrom		8. CONTRACT OR GRANT NUMBER(s) DAAG29-76-G-0238 MCS 77-01661
9. PERFORMING ORGANIZATION NAME & ADDRESS The Florida State University Department of Statistics Tallahassee, Florida 32306		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME & ADDRESS U.S. Army Research Office-Durham P.O. Box 12211 Research Triangle Park, N.C. 27709		12. REPORT DATE February, 1979 13. NUMBER OF PAGES 13
14. MONITORING AGENCY NAME & ADDRESS (if different from Contorlling Office)		15. SECURITY CLASS (of this report) Unclassified 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS

20. ABSTRACT

This article explains in general terms how some sequential bioassay methods like the stochastic approximation method or the up-and-down method are not in conformity with the likelihood principle. Irrespective of the sampling plan, the bioassay data may be analyzed in terms of the following simple prior probability model for the response probabilities.

Let $x_1' < x_2' < \ldots < x_m'$ be the distinct dosage levels used in a bioassay experiment and let $P_1 < P_2 < \ldots < P_m$ be the corresponding unknown response probabilities. Let $U_1 = P_1$ and $U_i = (P_i - P_{i-1})/(1 - P_{i-1})$, $i = 2, 3, \ldots m$. The U_i's are regarded as mutually independent random variables taking values in the unit interval. The P_i's then form a Markov chain. The means and the variances of the P_i's are related to those of the U_i's in a rather simple fashion. The case where $U_i \sim \text{Beta}(1, \lambda_i)$ is found to be particularly tractable for the analysis of bioassay data.